

### **REMARKS**

Claims 1-8, and 11, all of the pending claims in this application, are rejected in the Office Action dated December 5, 2008. Claim 1 has been amended merely to correct a typographical error. Claim 11 has been amended to recite that the fertility regulation is contraception in a female. Support for the amendments to claim 1 can be found on page 21, lines 1-3, of the specification. Applicants respectfully request reconsideration of the claims in view of the foregoing amendments and the following remarks.

#### **Claims are Enabled.**

Claims 1-8, and 11 are rejected under 35 U.S.C. §112, first paragraph, because, according to the Examiner, the specification, while enabling for the use of a particular example of the claimed compounds as contraceptives in females, does not reasonably provide enablement for other compounds and as such is not enabling for fertility regulation in either males or females, is not enabling for the use of the claimed compounds as contraceptives for males, and is not enabling for compounds other than those discussed in the declaration of Cornelius Marius Timmers filed October 3, 2008 (the "Timmers declaration"). The Examiner thus asserts that the specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with the pending claims. The Examiner asserts that in view of the data in the specification and the Timmers declaration that some compounds show agonist activity, others antagonist activity and yet others show both agonist and antagonist activity with respect to the FSH receptor and therefore predictability towards fertility regulation is very low. In addition, the Examiner asserts that Formula I includes variables which can be substituted with other variables, which in turn can be substituted with other variables resulting in a large number of very complex molecules encompassed by formula I. In view thereof, according to the Examiner even small structural modifications such as the addition of a single alkyl group can result in significant changes to the activity of the compounds and there is no guidance or working examples in the specification for the use of the claimed molecules *in vivo*. In response to applicants arguments regarding guidance in the specification for assays to determine activity of the claimed

compounds to the FSH the Examiner asserts that an undue burden exists where the skilled artisan would first need to synthesize a claimed compound, assay it for activity against the FSH receptor, and then correlate the *in vitro* activity with *in vivo* activity to establish effective treatment regimens.

In response applicants submit that the Examiner's rejection of the claims is directed to an alleged lack of enablement with respect to treating fertility in a patient. Applicants submit that claims 1-7 are directed to compounds and claim 8 to a composition comprising such compounds and do not require treating fertility. The specification and the "Timmers declaration" submitted previously clearly identify activity for each of the examples described in the application, either as agonist, antagonist or both for the FSH receptor. The examples provide for at least one working example of each of the different substituents for formula I as in the claimed invention. In a recent decision by the Board of Patent Appeals and Interferences application of the enablement requirements to compounds and compositions has been reviewed. See *Ex Parte Riedl*, Appeal 2008-3178 (BPAI, Sept. 23, 2008). The Board decided that where compounds and compositions are concerned the specification is required to enable one of skilled in the art to make the compounds and compositions and to provide some credible use. A sufficiently clear and detailed description is required to enable the skilled artisan to make the claimed compound or composition. However, in *Ex Parte Riedl* the Board determined that providing some credible use is all that is needed when the claimed invention is directed to compounds. Thus, applicants in *Ex Parte Riedl* were not required to show for each of the compounds claimed whether they would be successful in the treatment of osteoporosis. The Board reasoned that the claims were not directed to a method of treating osteoporosis and the claimed compounds were shown to have an effect on the kinase signalling pathway that is known to be linked with osteoporosis. Similarly to *Ex Parte Riedl*, the claimed invention in claims 1-8 is directed to compounds and compositions, the preparation for which has been clearly described in the specification to one of skill in the art both generally and through specific examples commensurate with the entire scope of the claimed invention. Further, as discussed these compounds and compositions have been shown to be either an agonist, antagonist or both for the FSH receptor (see also Timmers declaration), an important hormonal receptor linked to fertility. For these reasons, applicants submit that the specification clearly describes to one of skill in the art how to make the compounds and composition of the claimed invention and provides a

credible use therefore, having shown activity to the FSH receptor, a known receptor in regulating fertility. Thus, the compounds and compositions of claims 1-8 are clearly enabled by the specification to one of skill in the art.

With respect to claim 11, applicants have amended this claim to recite that the fertility regulation is contraception in woman. As previously discussed the specification provides antagonistic activity of the claimed compounds and compositions to the FSH receptor. As pointed out by the Examiner such decreased activity of the FSH receptor has been recognized in contraception in females. Enablement is not limited to particular working examples and the need for some experimentation is not enough to establish a lack of enablement as long as the required experimentation is reasonable (not undue). Applicants submit as previously presented that the specification provides clear guidance with respect to assaying antagonistic activity for the compounds of the claimed invention. See for example on page 17, line 28 to page 18, line 4 of the specification. Such antagonistic activity to the FSH receptor is also shown for the examples in the Timmers declaration. FSH receptor activation through FSH in women is a well described pathway in regulating fertility. Thus, applicants submit there is a clear nexus between the observed activity of the claimed tetrahydroquinoline derivatives of formula I as antagonist and a method of regulating fertility wherein the regulation of fertility is contraception in women. For these reasons, Applicants submit that the specification provides an enabling disclosure for the claimed tetrahydroquinoline derivatives of formula I describing a method for determining as well as showing inhibition of the FSH receptor activity and thereby also the corresponding decrease in fertility. Thus, Applicants submit that the skilled artisan reading the disclosure of the currently pending application would know how to make and/or use the claimed invention of amended claim 11, providing an enabling disclosure to the skilled artisan for where the regulation of fertility is contraception in females.

Accordingly, Applicants submit that claims 1-8, and 11 are clearly enabled by the specification as filed and respectfully request withdrawal of the rejection of claims 1-8, and 11 under 35 U.S.C. §112, first paragraph.

Double Patenting Rejection.

Claims 1-8 and 11 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1, 2, 9, 13, and 16 of co-pending application 10/540,336. Applicants defer responding to the rejection until such time as any of the above claims is allowed at which time applicants, although disagreeing with the Examiner's assertions, intend to submit a proper Terminal Disclaimer.

In view of the above amendment, Applicants believe the pending application is in condition for allowance. If the Examiner believes a telephone conference would be of value, she is requested to call the undersigned at the number listed below. Applicants respectfully request the issuance of a timely Notice of Allowance in the case.

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Organon International Inc.  
Patent Department  
c/o Schering-Plough Corporation  
2000 Galloping Hill Road  
Kenilworth, New Jersey 07033-0530  
K-6-1; MS 1990  
Tel: (908) 298-2161  
Fax: (908)-298-5388

Respectfully submitted,

By 

Susan Hess  
Registration No.: 37,350  
Attorney For Applicant(s)